DETAILED ACTION

Response to Amendments/Arguments

Applicant's amendments and arguments filed April 5, 2010 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below in original or modified form is herein withdrawn. While Applicant has amended the claims, Applicant has not overcome additional elements of the applied references that render the claims obvious. The rejection has been amended below to reflect how the rejection applies to the claims as amended.

Claims 1-13 and 15 are pending. Claims 1-7, 11 and 12 remain withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 1, 2008.

Applicant cites several court decisions as alleged support that the instant claims are non-obvious over the prior art. Applicant asserts that in light of *Takeda* and *Eisai* the there is a requirement of identifying a lead compound and that the prior art must suggested making the modifications to achieve the claimed invention and must have some reason to make the modifications. Applicant again argues the art teaches HIV inhibitors, while the instant compounds are contemplated as antiproliferatives and that modifications possible for treating HIV are not necessarily the same as those for use as an antiproliferative.

Respectfully, the examiner disagrees. The art clearly provides sufficient reason to achieve the instantly claimed compounds. Billich teaches the core structure and the possible modifications, i.e. a genus of compounds useful to treat HIV (e.g. claim 1; column 1, line 1 to

column 3, line 12). In fact, this genus of Billich (column 1, lines 1-35) is the same as that of withdrawn claim 1 (a 'use' claim). In contrast to Applicant's assertion that the "modifications used to arrive at the presently claimed compounds may not have been contemplated for treatment of HIV," the instant specification and original claims (including the use claim of claim 1) clearly indicates that the compounds of Billich are the same compounds as instantly claimed. Making any compound of Billich would have been expected by Billich to treat HIV, and in the instant application the expectation is that the same compound will treat a proliferative disorder. This is clearly the case when instant claim 1 is compared to the teachings of Billich. One would immediately recognize from the teachings of the art that any compound in the genus of Billich is expected to function in treating HIV, and would find ample teaching, suggestion and motivation to have made any of the compounds in that genus with the expectation that they would function to treat HIV. One would clearly look to the art to determine which elements would define the portions of Billich. Here, claim 8 is drawn only to a compound of formula I*. While the specification may assert a utility, the utility is not examined for patentability of the compound. The examiner is not required, as Applicant appears to assert, to determine obviousness in light of applicant's intended utility. The art has a different utility, and thus motivation to combine is found in that relevant art. In looking at the preferred embodiments of Billich, one clearly has a 'core structure' from which one would make modifications. Thus, as amended below, the rejection is maintained.

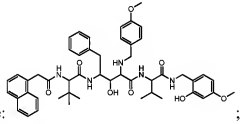
Further, new grounds of rejection are required in light of the amendments. Specifically, claim 9 and 10 are now rejected under 112 2nd.

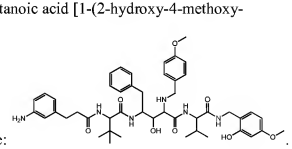
Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 lack clear antecedent basis. As amended, claim 8 does not provide support for R_5 = arylalkyl, pyridyl or alkyl or for Y = CO.

Claim 13 lacks antecedent basis. As amended, claim 8 no longer allows for Y = -CO- and does not provide antecedent support for the compound 4-[3,3-Dimethyl-2-(2-naphthalen-1-yl-acetylamino)-butyrylamino]-3-hydroxy-2-(4-methoxy- benzylamino)-5-phenyl-pentanoic acid [1-(2-hydroxy-4-methoxy-benzyl-carbamoyl)-2-methyl- propyl]-amide:  ; or

4-{2-[3-(3-Amino-phenyl)- propionylamino]-3,3-dimethyl-butyrylamino}-3-hydroxy-2-(4- methoxy-benzylamino)-5-phenyl-pentanoic acid [1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2- methyl-propyl]-amide:  .

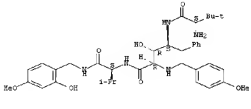
Claim Rejections - 35 USC § 103

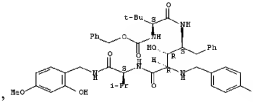
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

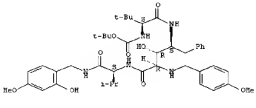
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-10, 13 and 15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over BILLICH (US Patent 5,538,997; IDS 2/26/02) in view of SCHOLZ (D. Scholz et al. J. Med. Chem. (1994) 37, pages 3079-3089).

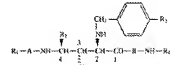
As stated in the instant specification, Billich teaches the instantly claimed compound where the only difference is the N-protecting group, e.g. compounds such as:



,


and


. (It is noted the N-terminus is at the right side of the compound as depicted)

Billich teaches that in the compounds of the structure:

, R_1 is an amino protecting group or is of the group R_5Y, where R_5 may be, amongst other options, substituted arylalkyl (column 1, lines 17-25). The compounds of Billich are contemplated as antivirals for HIV (e.g. column 1, lines 36-40).

Billich teaches that Y is preferably -CO- or -O-CO-, especially O-CO- (e.g. column 2, lines 14 and 15). R_5 is preferably optionally substituted alkyl, arylalkyl, or heteroaryl group with preferred being pyridylalkyl, 2-pyridylmethyl, benzyl-CH(OH)- and phenoxymethyl (e.g. column 2, lines 16-21). Further, aryl, heteroaryl and aryl parts of arylakyl may be mono or polycyclic such as pyridyl, naphthyl, FMOC, benzimidazolyl. Cycloalkylalkyl preferably is cyclohexylalkyl (e.g. column 2, lines 46-60).

Scholz teaches HIV antivirals, sharing the core structure of the instant compounds, providing structural analysis of the various positions and their effect on activity (throughout). Scholz determined that the N-terminal protecting group adversely affected the activity when changed from the aryl to alkyl groups, e.g. benzyl to t-butyl (e.g. page 3083, table 4 and discussion). Substitution with 2-pyridine produced a slightly better inhibitor. Scholz states that the R_1 group findings are consistent with the knowledge in the art the HIV P3 site has preference for aromatic residues.

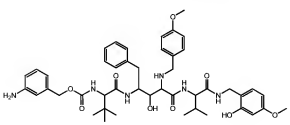
Thus, it would have been obvious to the artisan of ordinary skill in the art to have made any of the compounds of Billich, including those where Y = O-CO- and R_5 is cycloalkyl or naphthyl, with the expectation they would function as taught Billich to treat HIV. One would have been motivated to have made the compounds of Billich, as Billich teaches they can be used to treat HIV and teaches specifically that one can use -O-CO- and cycloalkyl and maphthyl as preferred species of the generic R_5. In light of the teachings of Scholz, one would have been motivated to have avoided alkyl protecting groups, however such teaching does not lead one to avoid other protecting groups. One would have had a reasonable expectation for success in

making the compounds, as Billich provides guidance and instruction on making the compounds and chemical synthesis is a technique widely practiced in the synthetic chemical arts.

Obviousness does not require absolute predictability, only a reasonable expectation of success, i.e., a reasonable expectation of obtaining similar properties. See, e.g., *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Here, there is ample teaching to provide a reasonable expectation that the compounds of Billich will have similar properties, all being useful for treating HIV.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Allowable Subject Matter

The compound:  (claim 13) is free of the prior art, and is not taught or suggested by the art of record.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 1-7, 11 and 12 drawn to an invention nonelected without traverse in the reply filed on April 1, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREW D. KOSAR whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654